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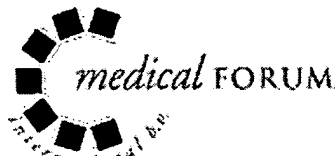
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Oral contraceptives in the treatment of acne

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Introduction

Acne is a disease of the sebaceous glands that develops during puberty and often improves after puberty. The activity of the sebaceous glands is stimulated by androgens and inhibited by estrogens [1]. The occurrence of **acne** coincides with increasing androgen levels in the young individual. However, the improvement of **acne** after puberty does not reflect a counter change in the hormonal pattern. The majority of patients with **acne** have normal circulating levels of androgens. In women with severe **acne**, low circulating levels of sex hormone-binding globulin (SHBG), the testosterone-binding protein, have been reported together with normal testosterone, possibly reflecting an increased production and turnover rate of testosterone [2]. Since **acne** only affects some individuals it is reasonable to propose that there is an increased local sensitivity to androgens in the sebaceous glands in those who are affected [3]. It has also been suggested that in individuals with **acne**, there is an increased conversion in the skin of testosterone to the more potent androgen, dihydrotestosterone [4]. To summarise, androgens are involved in the development of **acne**, but androgenic disorders are unlikely to be the main aetiological factor behind most cases of **acne**. In the female, androgens are produced both from the ovaries and from the adrenals. Consequently, drugs that inhibit ovulation also reduce ovarian androgen production to some extent.

Because sex steroids are involved in the development of **acne**, suggesting increased androgen activity/sensitivity as an aetiological factor, antiandrogenic drugs have been tried for the treatment of **acne**.

Estrogens, progestogens and antiandrogens in oral contraceptives

The combined oral contraceptive pill (OCP) contains a potent estrogen, ethinylestradiol (EE), and a progestogen. To date, most progestogens in combined OCPs have been derivatives of 19-nortestosterone. Although these progestogens are not true androgens, they have varying degrees of binding capacity to the androgen **receptor** and thereby exert varying degrees of weak androgenic effects, depending on the type and dose of progestogen [5]. The antiandrogenic effect of a combined OCP is therefore a result of both the decreased synthesis of endogenous androgens and the balance between the estrogenic effects of EE and the androgenic/antiestrogenic effects of the progestogen. In addition, combined OCPs increase SHBG levels, thus binding more circulating testosterone and reducing its availability to the tissues. All currently available combined OCPs contain EE and most of those that are commonly used contain around 30 mg EE. Among currently available progestogens, the 'second-generation' progestogens, e.g. levonorgestrel and norethisterone, have been reported to bind to the androgen **receptor** as well as to the **progesterone receptor**, whereas 'third-generation' progestogens, e.g. desogestrel, norgestimate and gestodene, bind more selectively to the **progesterone receptor** [5].

Antiandrogens are defined as substances that prevent androgenic effects, either by blocking the **receptor** or by interfering with androgen metabolism. Several steroids exert antiandrogenic effects, the most potent antiandrogen probably being estrogen. One of the antiandrogenic mechanisms of estrogen is to increase SHBG levels. Other steroid hormones that have been associated with antiandrogenic effects are spironolactone and cyproterone acetate (CPA). CPA is a derivative of hydroxyprogesterone and acts as a progestogen and as an antiandrogen [6]. CPA has been used in combination with different doses of EE for the treatment of androgenic disorders. Spironolactone given orally in a dose of 200 mg daily has also been shown to have antiandrogenic effects, reducing sebum excretion rate and improving **acne** [7]. When given to women, spironolactone alone has been reported to cause menstrual irregularities [7]. Recently, a progestogen derived from spiro lactone with anti-androgenic and anti-mineralocorticoid properties has been developed, drospirinone, and used in the first OCP [8]. The progestogenic effects of drospirinone are claimed to be similar to those of natural **progesterone** and the combined preparation to be favourable in women with **acne**, but, as yet, no randomised comparative study addressing this issue has been published [8].

Clinical studies of combined oral contraceptives in acne

Several studies have tried to evaluate the effect of combined oral contraceptives on **acne**. Below are reported only studies that were randomised and compared different regimens.

There has been only one placebo-controlled, randomised, double-blind trial studying the effects of a combined OCP preparation on **acne** [9]. This study evaluated the effect of a triphasic combined OCP containing norgestimate (0.180 mg on days 1-7, 0.215 mg on days 8-14, and 0.250 mg on days 15-21) together with a fixed dose of 35 mg EE (n = 84) against placebo (n = 80) in women with moderate **acne vulgaris** for 6 months [9]. The number of lesions decreased in both groups, though more significantly so in the combined OCP group. The general improvement of **acne** was also statistically significantly in favour of the combined OCP, both when assessed by the patients and by the investigators. The endocrine parameters tested were as expected in the treatment group, with a threefold

increase in SHBG and a decrease in both free testosterone and dehydroepiandrosterone sulphate, whereas total testosterone did not decrease. In another study, women with **acne** were randomly allocated to one of three treatment groups, all receiving the same dose of EE (50 mg) together with either CPA 50 mg, CPA 2 mg or norethisterone 1 mg. Patients were assessed for the severity of symptoms of **acne** by grading, lesion count and photography. In addition, sebum excretion rate, bacterial counts and hormone levels were measured. After 6 months, clinical improvement was found in all groups, but a significantly more rapid and pronounced response was seen in the groups receiving CPA. There was a trend for a more pronounced response among those who received the high dose of CPA, but the difference between these patients and those receiving the low CPA dose was not statistically significant [10]. Another study randomly allocated patients to one of three groups: one group received CPA 2 mg + EE 50 mg alone, another received the same medication in combination with tetracycline 500 mg daily, while a third group received the same dose of tetracycline alone [11]. After 6 months, all groups had improved; however, the group that had received the combined treatment (CPA/EE + tetracycline) showed significantly more improvement than the other groups. There was no significant difference between those receiving hormonal treatment alone and those receiving tetracycline alone, except that the patients in the latter group deteriorated more rapidly after the end of the 6 treatment months and showed significantly worse signs of **acne** 2 months after treatment than did those who had received hormones.

One study compared CPA in combination with either 35 mg or 50 mg of EE and reported no difference after 6-12 months of treatment with regard to effects on **acne**, both doses being highly effective [12].

Carlborg [13] studied women who were randomly assigned to either CPA/EE (2 mg/50 mg), CPA/EE (2 mg/30 mg) or levonorgestrel/EE (150 mg/30 mg). After 6 months, all three groups had improved significantly compared with pretreatment, the two CPA groups being significantly better than the levonorgestrel group.

An open randomised study compared CPA/EE (2 mg/35 mg) with desogestrel/EE (150 mg/30 mg) and reported significantly better results with the CPA/EE preparation after 9 months, especially with regard to facial **acne** and effects on seborrhoea [14].

Palatsi et al. [15] studied the effects of two different combined OCPs, desogestrel/EE (150 mg/30 mg) and levonorgestrel/EE (150 mg/30 mg) on **acne**, serum free testosterone and SHBG. **Acne** improved in both groups, albeit significantly more in the desogestrel group. The authors noted a 60% reduction in free testosterone in both groups and a significant increase in SHBG in the desogestrel but not in the levonorgestrel group.

One open randomised study compared a biphasic preparation containing desogestrel/EE (25 mg/40 mg on days 1-7 and 125 mg/30 mg on days 8-22) with CPA/EE (2 mg/35 mg) during four treatment cycles [16]. A reduction in the number and severity of lesions was found in both groups and there was no difference between the groups.

Conclusion

All oral contraceptive preparations containing an estrogen/progestogen combination seem to improve **acne**. Therefore, although **acne** is not the primary indication for combined OCPs, it seems reasonable to recommend a combined OCP to women suffering from **acne**, particularly if they also require a

contraceptive method. There is reasonable evidence from comparative clinical studies that good improvement of **acne vulgaris** particularly follows treatment with desogestrel/EE or norgestimate/EE and with the only labelled anti-**acne** OCP containing CPA/EE.

References

1. Cunliffe WJ, Bottomley WW. Antiandrogens and **acne**. A topical approach? *Arch Dermatol* 1992; 128: 1261-4.
2. Schmidt JB, Lindmaier A, Spona J. Endocrine parameters in **acne vulgaris**. *Endocrinol Exp* 1990; 24: 457-64.
3. Harris HH, Downing DT, Stewart ME, Strauss JS. Sustainable rates of sebum excretion in **acne** patients and matched normal subjects. *J Am Acad Dermatol* 1983; 8: 200-3.
4. Cunliffe WJ. **Acne**. London: Martin Dunitz, 1989.
5. Bergink EW, Kloosterboer HJ. Structural requirements for optimal **receptor** binding of contraceptive progestogens [abstract]. *Adv Contracept* 1985; 1: 256.
6. Neumann F. Pharmacological aspects of cyproterone acetate. In: Schindler AE, ed. *Antiandrogen-estrogen therapy for signs of androgenization*. Berlin: Walter de Gruyter, 1987; 23-40.
7. Burke BM, Cunliffe WJ. Oral spironolactone therapy for female patients with **acne**, hirsutism or androgenic alopecia [letter]. *Br J Dermatol* 1985; 112: 124-5.
8. Boschitsch E, Skarabis H, Wuttke W, Heithecker R. The acceptability of a novel oral contraceptive containing drospirinone and its effects on well-being. *Eur J Contracept Reprod Health Care* 2000; 5 (3 suppl): 34-40.
9. Lucky AW, Henderson TA, Olson WH, et al. Effectiveness of norgestimate and ethinyl estradiol in treating moderate **acne vulgaris**. *J Am Acad Dermatol* 1997; 37: 746-54.
10. Miller JA, Wojnarowska FT, Dowd PM, et al. Anti-androgen treatment in women with **acne**: a controlled trial. *Br J Dermatol* 1986; 114: 705-16.
11. Greenwood R, Brummit L, Burke B, Cunliffe WJ. **Acne**: double blind and laboratory trial of tetracycline, oestrogen-cyproterone acetate, and combined treatment. *Br Med J* 1985; 291: 1231-5.
12. Fugère P, Percival-Smith RK, Lussier-Cacan S, et al. Cyproterone acetate/ethinyl estradiol in the treatment of **acne**. A comparative dose-response study of the estrogen component. *Contraception* 1990; 42: 225-34.
13. Carlborg L. Cyproterone acetate versus levonorgestrel combined with ethinyl estradiol in the treatment of **acne**: results of a multi-center study. In: Schindler AE, ed. *Antiandrogen-estrogen therapy for signs of androgenization*. Berlin: Walter de Gruyter, 1987; 191-6.
14. Erkkola R, Hirvonen E, Luikku J, et al. Ovulation inhibitors containing cyproterone acetate or desogestrel in the treatment of hyperandrogenic symptoms. *Acta Obstet Gynecol Scand* 1990; 69: 61-5.
15. Palatsi R, Hirvensalo E, Liukko P, et al. Serum total and unbound testosterone and sex hormone binding globulin (SHBG) in female **acne** patients treated with two different oral contraceptives. *Acta Derm-Venereol* 1984; 64: 517-23.
16. Dieben TO, Vromans L, Theeuwes A, Coelingh Bennink HJ. The effects of CTR-24, a biphasic contraceptive combination, compared to Diane-35 in women with **acne**. *Contraception* 1994; 50: 373-82.

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